Abstract No. evan492

Single Crystal Studies of PZ-Immucillin-H

G. Evans, R. Furneaux, G. Gainsford, P. Tyler (Industrial Research Limited, New Zealand), V. Schramm (Albert Einstein College of Medicine), J. Hanson and J. Larese (BNL)

Beamline(s) X7B

Introduction: The pyrazolo-derivative of Immucillin H, (1S)-1,4-dideoxy-1-*C*-(7-hydroxypyrazolo[4,3-*d*]pyrimidin-3-yl)-1,4-imino-D-ribitol, was designed to mimic the transition state adopted by inosine on phosphorolysis catalyzed by the enzyme purine nucleoside phosphorylase (PNP). It is the most potent inhibitor of the human form of this enzyme discovered to date, with a K_i* = 7 picomolar. This crystal structure was undertaken in order to confirm the structure of this synthetic, microcrystalline material and to provide co-ordinates for comparison with anticipated data from enzyme-inhibitor complex structures.

Methods. $2(C_{10}H_{13}N_5O_4)^+.2Cl^-.H_2O$, monoclinic space group $P2_1$, a=14.040(5), b=7.000(5), c=14.884(5) Å; β= 116.112(5)º; V= 1313.5(11) $Å^3$; Z = 2; D_c = 1.576 $g.cm^{-3}$; T = 293(2) K; λ (synchrotron) = 0.93000 Å; μ = 0.319 mm^{-1}. Data were collected with a MAR345 image plate detector on a two small crystals (0.125 x 0.010 x 0.010 mm). The structure was solved by direct methods and refined on F^2 using all data to give R_1, wR_2 = 0.0993, 0.265(all data).

Results: The packing of the two molecules is shown in the figure below.

Acknowledgements: The work at NSLS was supported under contract DE-AC02-98CH10886 with the US DOE Office of Basic Energy Sciences.